=DOCKET NO.: ISIS-4804

PATENT

APR 0 8 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re Application of:

Manoharan, et al.

Serial No.: 09/996,292

Group Art Unit: Not yet assigned

Filing Date: 3/13/02

Examiner: Not yet assigned

For: Nuclease Resistant Chimeric Oligonucleotides

I, Jane E. Inglese, Registration No. 48,444 certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

On March 29, 2002 Opene Suglese

U. S. Patent and Trademark Office

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STATEMENT TO SUPPORT FILING AND SUBMISSION IN ACCORDANCE WITH 37 CFR §§ 1.821 THROUGH 1.825

	I hereby state, in accordance with the requirements of 37 C.F.R. §1.821(f), that the contents of the paper and computer readable copies of the Sequence Listing, submitted in accordance with 37 CFR §1.821(c) and (e), respectively are the same.
<u> </u>	I hereby state that the submission filed in accordance with 37 CFR §1.821(g) does not include new matter.
	I hereby state that the submission filed in accordance with 37 CFR §1.821(h) does not include new matter or go beyond the disclosure in the international application as filed.
	I hereby state that the amendments, made in accordance with 37 CFR §1.825(a), included in the substitute sheet(s) of the Sequence Listing are supported throughout the application, as filed. I hereby state that the substitute sheet(s) of the Sequence Listing does (do) not include new matter.

DOCKET NO.: ISIS-4804

-2
I hereby state that the substitute copy of the computer readable form, submitted in accordance with 37 CFR §1.825(b), is the same as the amended Sequence Listing.

I hereby state that the substitute copy of the computer readable form, submitted in accordance with 37 CFR §1.825(d), contains identical data to that originally filed.

Date: March 29, 2002

Date: March 29, 2002

Date: March 29, 2002

Date: March 29, 2002

Woodcock Washburn LLP One Liberty Place - 46th Floor Philadelphia PA 19103 Telephone: (215) 568-3100

Facsimile: (215) 568-3439

C 2001 WW



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Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be submitted using one of the following methods:

1. Electronically submitted through EFS-Bio (http://www.uspto.gov/ebc/efs/downloads/documents.htm, EFS Submission User Manual - ePAVE)

2. Mailed to:

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BORN AMERICAN

RAW SEQUENCE LISTING

APR 0 8 2002



The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number:	09/996,292	
Source:	3910	
Date Processed by STIC:	12/6/01	

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION QUESTIONS, PLEASE CONTACT MARK SPENCER, 703-308-4212.

FOR SEQUENCE RULES INTERPRETATION, PLEASE CONTACT ROBERT WAX, 703-308-4216. PATENTIN 2.1 e-mail help: patin21help@uspto.gov or phone 703-306-4119 (R. Wax) PATENTIN 3.0 e-mail help: patin3help@uspto.gov or phone 703-306-4119 (R. Wax)

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE <u>CHECKER</u> <u>VERSION 3.0 PROGRAM</u>, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW:

Checker Version 3.0

The Checker Version 3.0 application is a state-of the-art Windows based software program employing a logical and intuitive user-interface to check whether a sequence listing is in compliance with format and content rules. Checker Version 3.0 works for sequence listings generated for the original version of 37 CFR §§1.821 – 1.825 effective October 1, 1990 (old rules) and the revised version (new rules) effective July 1, 1998 as well as World Intellectual Property Organization (WIPO) Standard ST.25.

Checker Version 3.0 replaces the previous DOS-based version of Checker, and is Y2K-compliant. Checker allows public users to check sequence listings in Computer Readable form (CRF) before submitting them to the United States Patent and Trademark Office (USPTO). Use of Checker prior to filing the sequence listing is expected to result in fewer errored sequence listings, thus saving time and money.

Checker Version 3.0 can be down loaded from the USPTO website at the following address: http://www.uspto.gov/web/offices/pac/checker



Sequence Listing Error Summary

ERROR DETECTED SUGGESTED CORRECTION SERIAL NUMBER: 09 1996, 292

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE Wrapped Nucleics The number/text at the end of each line "wrapped" down to the next line. This may occur if your file Wrapped Aminos was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping." Invalid Line Length The rules require that a line not exceed 72 characters in length. This includes white spaces. The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers: Misaligned Amino Numbering use space characters, instead. Non-ASCII The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text. Variable Length contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing. A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid PatentIn 2.0 "bug" sequences(s) . Normally, Patentin would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences. Skipped Sequences Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence: (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) (OLD RULES) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading) (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) This sequence is intentionally skipped Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences. Skipped Sequences Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence. (NEW RULES) <210> sequence id number <400> sequence id number 000 Use of n's or Xaa's Use of n's and/or Xaa's have been detected in the Sequence Listing. (NEW RULES) Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents. 10 Invalid <213> Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or Response scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence Sequence(s) missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section. (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules) PatentIn 2.0 Please do not use "Copy to Disk" function of Patentln version 2.0. This causes a corrupted file, "bug" resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.

AMC - Biotechnology Systems Branch - 06/04/2001



OIPE

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/996,292

DATE: 12/06/2001 TIME: 11:33:45

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Output Set: N:\CRF3\12062001\1996292.raw

Does Not Comply
Corrected Diskette Needed

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       5 <120> TITLE OF INVENTION: Nuclease Resistant Chimeric Oligonucleotides
       7 <130> FILE REFERENCE: ISIS-4804
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C--> 9 <141> CURRENT FILING DATE: 2001-11-28
      9 <160> NUMBER OF SEQ ID NOS: 55
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     11 <170> SOFTWARE: PatentIn version 3.1
                                                                the Sequence Listing. Please check subsequent
     13 <210> SEO ID NO: 1
                                                                sequences for similar errors.
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     15 <212> TYPE: DNA
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                                                     - involid response, see error summary
Sheet, item 11
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RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/996,292

DATE: 12/06/2001 TIME: 11:33:45

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Output Set: N:\CRF3\12062001\I996292.raw

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RAW SEQUENCE LISTING PATENT APPLICATION: US/09/996,292

DATE: 12/06/2001 TIME: 11:33:45

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Output Set: N:\CRF3\12062001\1996292.raw

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RAW SEQUENCE LISTING

7 mg

DATE: 12/06/2001

PATENT APPLICATION: US/09/996,292

TIME: 11:33:45

17

17

Input Set : A:\ISIS4804.ST25.txt

Output Set: N:\CRF3\12062001\I996292.raw

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RAW SEQUENCE LISTING

to

DATE: 12/06/2001

PATENT APPLICATION: US/09/996,292 TIME: 11:33:45

Input Set : A:\ISIS4804.ST25.txt

Output Set: N:\CRF3\12062001\I996292.raw

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VERIFICATION SUMMARY

PATENT APPLICATION: US/09/996,292

DATE: 12/06/2001 TIME: 11:33:46

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Output Set: N:\CRF3\12062001\I996292.raw

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VERIFICATION SUMMARY

DATE: 12/06/2001

PATENT APPLICATION: US/09/996,292

TIME: 11:33:46

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Output Set: N:\CRF3\12062001\I996292.raw

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A Same